REMARKS

Reconsideration of the rejections set forth in the Office action mailed July 1, 2003 is respectfully requested. Claims 1-19 are currently under examination.

I. The Invention

A. The Claims

The applicant's invention, as embodied in independent claim 1, is directed to a method of injecting a liquid sample into an electrolyte channel in a microfluidics device. As recited in the claim, the device has a channel network that includes an electrolyte channel having upstream and downstream channel portions and first, second, and third side channels that intersect the electrolyte channel between the two channel portions at first, second, and third ports, respectively. At least one of the ports is axially spaced along the electrolyte channel from the other two ports. The method comprises the steps of:

(a) supplying a sample to the first side channel,

(b) applying across the first side channel and at least one of the other side channels, a voltage potential effective to move sample in the first channel into a volume element of the electrolyte channel, said volume element extending between the first port and at least one other port which is axially offset from the first port,

(c) simultaneously controlling the voltage applied to the three side channels, to create a sample volume element in the electrolyte channel having a desired leading- and trailing-edge shape and/or distribution of sample components, and

(d) simultaneously controlling the voltage applied to the upstream and downstream channel portion, and to at least two of the side channels, to advance this sample element in a downstream direction within the electrolyte channel.

Applicants wish to note that the Examiner's characterization of the "claimed method of using three electrodes on and one floating" (page 4 of the Office Action) is a misrepresentation of the claimed invention, as embodied in claim 1 above.

Independent claim 13 is directed to a microfluidic system designed for use in injecting a defined-volume liquid sample into an electrolyte channel, for transport through the channel. The system comprises:

a microfluidic device having a channel network that includes such an electrolyte channel having upstream and downstream channel portions and first, second, and third side channels that intersect the electrolyte channel between the two channel portions at first, second, and third ports, respectively, where at least one of the ports is axially spaced along the electrolyte channel from the other two ports,

ports for supplying liquid medium to the electrolyte channel and the side channels,

upstream and downstream electrodes, and first, second, and third electrodes adapted to communicate with liquid medium contained in upstream and downstream portions of the electrolyte channel, and the first, second, and third side channels, respectively, and

a voltage controller, which operates to:

(a) apply across the first side channel and at least one of the other two side channels, a voltage potential effective to move a liquid sample contained in the first channel into a volume element of the electrolyte chamber extending between the first and at least one other port which is axially offset from the first port,

(b) simultaneously control the voltage applied to the three side channels, and at least one of said upstream and downstream channel end portions, to create a sample volume element in the electrolyte channel that has a desired leading- and trailing-edge shape and/or distribution of sample components within the volume elements, and

(c) simultaneously control the voltage applied to the upstream and downstream channel portion, and to at least two of the side channels, to advance the sample element having a desired leading- and trailing-edge shape and/or distribution of sample components in a downstream direction within the electrolyte channel.

B. Features and Benefits of the Invention

Figures 1-3 of the specification illustrate three possible embodiments of a "channel network that includes an electrolyte channel having upstream and downstream channel portions and first, second, and third side channels [five channels in all] that intersect the electrolyte channel

between the two channel portions at first, second, and third ports, respectively", where "at least one of the ports is axially spaced along the electrolyte channel from the other two ports", as recited in claims 1 and 13. Figures 1-3 and 4A also illustrate one embodiment of sample loading and injection according to the claimed method, where "the voltage applied to the three side channels, and at least one of said upstream and downstream channel end portions" is simultaneously controlled "to create a sample volume element in the electrolyte channel that has a desired leading- and trailing-edge shape and/or distribution of sample components within the volume elements", as recited in claims 1 and 13.

One such embodiment is described, for example, at pages 11-13 of the specification, under the heading "A. Defined-volume sample injection". In particular, at page 11, line 29 to page 12, line 3, and page 12 lines 30-33, with reference to Fig. 1: "the control unit operates to apply a DC voltage potential <u>across the first side channel and each of the second and third side channels</u>, to move sample material from sample reservoir 38 into and through the electrolyte channel between ports 34, 36, and into the second <u>and</u> third side channels as shown....At the same time, as part of the sample-loading step, a voltage potential is applied to the upstream and downstream portions of the electrolyte channel, to move buffer or buffer ions in reservoirs 20, 24 toward and into side channels 28, 30....As seen in Fig. 1, the sample-loading steps are effective to move a defined-volume sample plug 90 into the electrolyte channel, and confine the leading and trailing edges thereof to well-defined boundaries just inside the respective side-channel ports." (emphasis added). As stated at page 13, lines 26-32, "This five-channel configuration, with simultaneous control at each of the five channels during sample loading and sample injection, has important advantages over simple channel-cross or double-T configurations that are known in the prior art. In particular, the system allows for precisely defined sample volumes that are shaped (have sharp interface boundaries) at both upstream and downstream sample volume edges. In this way, precisely known volumes of sample can be metered into the electrolyte channel."

Figures 5 and 6 illustrate embodiments of the method which employ transient ITP stacking of the sample, e.g. where sample including leading edge ion is injected between two regions of trailing edge buffer (Figure 5A). As described at page 14, line 32 to page 15, line 2, sample loading is carried out "in accordance with the method described with respect to Fig. 1...the

trailing-ion buffer is directed into the second [and] the third side channels during sample injection, to form sharp edge boundaries of the sample volume, indicated at 96."

Alternatively, the third side channel can be used to deliver the leading edge buffer, as illustrated in Figure 6.

A further embodiment of the method is illustrated in Fig. 7 and described on pages 17, line 21 to page 19, line 10. For example, as described at page 17, line 25 to 32, sample is injected from the sample channel into the electrolyte channel and a second side channel, "by applying a DC voltage potential <u>across the first and second channels</u>", and, "<u>at the same time...an AC voltage is applied across the third channel 30 and...the upstream channel portion</u>, as illustrated in Fig. 7B" (emphasis added). As noted at page 19, lines 5-10: "The sample-concentration method provides significant advantages over dielectric focusing methods proposed in the prior art. In particular, by providing a third, remote side channel that is not involved in sample movement, dielectric sample-component focusing can occur at a selected region adjacent the sample volume and at a position remote from the sample volume, allowing sample concentration at one region only."

As shown and described, the methods involve the use of a five-channel system, having upstream and downstream electrolyte channel regions and <u>three</u> side channels, where voltage is controlled simultaneously at the <u>three</u> side channels and at least one of the upstream and downstream channels. These methods provide advantages such as defined volume sample elements with sharp boundaries at both the upstream and downstream ends (see e.g. Figure 1 and page 13, lines 29-32, or page 15, lines 1-2), or the ability to concentrate sample at particular regions within the electrolyte channel (as illustrated in Figs. 7B-C and noted at page 19, lines 5-10).

II. <u>Rejections under 35 U.S.C. §102(b)</u>

Claims 1-9 and 13-17 were rejected under 35 U.S.C. §102(b) as being anticipated by Ramsey *et al.*, U.S. Patent No. 5,858,187. This rejection is respectfully traversed for the following reasons.

A. <u>The Prior Art</u>

Ramsey *et al.* is directed to methods of capillary electrophoresis in which sample is

transported from a sample reservoir to a "focusing chamber" (column 4, lines 10-12). At the focusing chamber, streams of buffer, electrodynamically transported from two laterally placed "focusing reservoirs", are used to laterally focus or confine the sample (column 4, lines 15-16, 35-38). This process is shown in Figs. 2, 4, and 14 of the patent.

Referring again to applicants' claim 1, the channel network of the claims includes "an electrolyte channel having upstream and downstream channel portions and first, second, and third side channels <u>that intersect the electrolyte channel between the two channel portions, at first, second, and third ports, respectively", where "at least one of the ports is axially spaced along the electrolyte channel from the other two ports</u>". Therefore, at least one "side channel" must intersect the electrolyte channel at a point which is "axially spaced" from the intersection point(s) of the other two "side channels".

By this definition, the channels leading to **14**, **16**, **20**, and **22** in Fig. 1 of Ramsey can be considered four "side channels". However, by this definition, four channels emanating from a single cross point, as in Figures 2, 4, and 14 of Ramsey, <u>cannot</u> include three "side channels".

The system shown in Fig. 1 of Ramsey can thus be said to have four "side channels", leading to reservoirs **14**, **16**, **20**, and **22**. However, as described at column 2, lines 15-19 and 28-30: "The invention entails using the focusing reservoirs **20** and **22** to laterally focus the sample transported from sample reservoir **12** to waste reservoir **18**. The electric potentials at the sample reservoir **12**, and focusing reservoirs **20** and **22**, are controlled independently. <u>No potential is applied to the buffer and sample waste reservoirs **16** and **14**</u>; *i.e.,* the reservoirs are electrically floated" (emphasis added). Accordingly, voltage is controlled at only <u>two</u> of the "side channels" during the processes described.

In view of this description, the reference does not show "simultaneously controlling the voltage applied to [the] three side channels" (element (c) of applicants' claims 1 and 13).

Since the reference does not disclose all of the elements set out above in independent claims 1 and 13 and their dependent claims, these claims cannot be anticipated by this reference under 35 U.S.C. §102(b). In view of this, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §102(b).

Nor the does the reference <u>suggest</u> methods in which voltage is applied to three "side

channels", as claimed, is simultaneously controlled. There is no disclosure or suggestion of the sample loading and injection methods claimed and described in applicants' specification, which are effective, for example, to provide sample volume elements having controlled volumes and sharp boundaries at both the upstream and downstream ends (e.g. Figs. 1-3, 4A, 5A), or to dielectrically concentrate sample at a precise region (e.g. Fig. 7B). There is no suggestion of how the process illustrated in Figs. 2, 4, and 14 of Ramsey could be used to provide these benefits.

III. Rejections under 35 U.S.C. §103

Claims 10-12 and 18-19 were rejected under 35 U.S.C. §103 as being unpatentable over Ramsey *et al.*, cited above, in view of Chow *et al.*, U.S. Patent No. 6,174,675. The rejections are respectfully traversed in light of the following remarks.

A. The Invention

The invention of independent claim 1 and of independent claim 13 is described above. Dependent claims 10-12 and 18-19 further provide that step (b) includes applying a DC voltage potential across the first and second side channels, and step (c) includes applying an AC voltage between the third side channel and an upstream or downstream channel portion. As shown in Fig. 7B and described in the paragraph bridging pages 17-18 of the specification, and the second full paragraph of page 19, the alternating voltage field is effective to produce dielectric focusing of sample components at a precise region within the sample volume element.

B. The Cited Art

Ramsey *et al.* is described above.

Chow *et al.* describes the use of electrical current for controlling and/or monitoring fluid parameters, particularly temperature, in microchannels. As noted at, for example, column 16, lines 38-41, "electroosmotic or electrophoretic forces", among others, can be used to move materials through the channels. However, as shown by the Summary of the Invention at columns 3-5, the various aspects of the invention are primarily concerned with the use of electric current within microchannels to control and/or monitor fluid temperature. Every paragraph in the lengthy Summary of the Invention is in some sense concerned with heating or temperature

control. For example, at column 3, lines 49-51: "The energy source provides a voltage across the fluid such that a portion of a fluid is heated in a portion of the capillary channel."

The use of alternating and direct current is discussed at column 17, lines 31-63 of the patent. The reference teaches that, while both can be used for heating (e.g. lines 34-36, 45), AC can be used "to heat the material...without adversely affecting the movement of that material" (lines 40-42, 48-50). This is reiterated in Example 2, directed to a thermal cycling reaction, which states that use of an AC power source prevented electroosmotic flow of material, while a DC power supply could be used to electroosmotically transport materials (and to heat the materials, as stated at lines 22-24).

Conventional channel networks are shown and briefly described in the reference (e.g. "T intersections, cross intersections, wagon wheel intersections", and the "basic cross channel structure"; column 10, lines 30-41, also referred to as the "four way, cross intersection"; column 11, line 30). However, there is nothing in the reference pertaining to simultaneous control of voltages at the three side channels of a network as recited in the applicant's claims (i.e. including an electrolyte channel having upstream and downstream channel portions and first, second, and third side channels that intersect the electrolyte channel between the two channel portions at first, second, and third ports, respectively, where at least one of the ports is axially spaced along the electrolyte channel from the other two ports), using both AC and DC voltage as claimed, to produce dielectric focusing.

C. Analysis

Since Chow describes the use of alternating current in a microfluidic device for the purpose of heating fluid material, without producing electroosmotic flow, there would be no motivation to apply the technique to the Ramsey system, which is concerned with controlled flow and separation of materials. The Ramsey reference does not provide any suggestion that one would wish to use electric current for heating in the systems described.

Moreover, the references, even if combined, do not suggest the claimed invention. As noted above, the applicants' independent claims include at least one element not taught by Ramsey or Chow; that is, the aspect of "simultaneously controlling the voltage applied to [the] three side channels" in the process of injecting a sample into a separation channel. The teachings of Chow

regarding temperature control in microchannels do not make up for this deficiency.

In view of the foregoing, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §103.

IV. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

No further fees are believed due with this communication. However, the Commissioner is hereby authorized and requested to charge any deficiency in fees herein to Deposit Account No. 50-2207.

If in the opinion of the Examiner a further telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4403.

Respectfully submitted,

LeeAnn Gorthey

LeeAnn Gorthey
Registration No. 37,337

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Correspondence Address:
PAYOR NUMBER 22918
PHONE: (650) 838-4403
FAX: (650) 838-4350